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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,295	04/05/2007	Donald W. Kufe	GENU:006US/10717023	2459

32425 7590 10/06/2010

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
10/06/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

aopatent@fulbright.com

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/598,295	KUFE ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 September 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *23 September 2010*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☒ Other: See Continuation Sheet.

/Sean R McGarry/
Primary Examiner, Art Unit 1635

Continuation of 11. does NOT place the application in condition for allowance because: The declaration filed under 37CFR 1.131 by Donald W. Kufe has been considered. The weight of the evidence provided in the declaration is of insufficient weight to overcome the rejection of record. The declaration is drawn to a discussion of how antisense compounds work by a different mechanism and an assertion that since an antisense target may not predict an siRNA target on a gene, one would not expect that an siRNA can be targeted to a gene known to be targeted by antisense. This position is not agreed with and further explaination is provided in response to applicant arguments. . Applicant Argues that there is no motivation and argues that Tuschl et als' teachings provide no guarantee that siRNA will work the same in all sytems (applicant is reminded that the prior art needs to provide a reasonable expectation of success and not a gaurantee). Applicant then asserts that "It is critical to note that the Tuschl data are in D. melanogaster-not even a mammalian system, and certainly not in human cells. Applicant is simply mistaken. While the Tuschl reference does indeed provide data from D. melanogaster, there is also mammalian data and even human cell data. The paragraph 148 that the examiner specificly pointed to in the rejection of record, is in Example 2, which is titled "RNA Interference in Human Tissue Cultures". Applicant may also refer to paragraphs 7, 29,137, 148, and 177, and FIG9, FIG10, FIG19, for example. The examiner did point to paragraph 148 where is was observed the enhanced activity in human cells when siRNA is compared to antisense or ribozymes. At paragraph 137 it is stated that ". . the siRNA duplexes represent a new alternative to antisense or ribozyme therapeutics." Applicant then argues a lack of likelyhood of success and argues that antisense work by different mechanism than siRNA and that a siRNA may not correlate well with an known antisense compound. Applicants strawman argument about the lack of correlation between specific compounds is indeed not on point. It is clear that siRNA would be substituted by one in the art NOT made from and antisense of the prior art. Tuschl provides ample teachings for the design of siRNA compounds that will inhibit a target gene. Refering to the Miyagashi reference, applicant asserts that their results showed that there were significant differences in the suppressive effects at each of the target sites and that one of ordinary skill in the art would have understood that the effects of antisense technology are not necessarily the same as the effects with RNA interference. The reference does show differences, however it should really be noted that both antisense and siRNA inhibited the same gene. It is noted that the most potent antisense and the most potent siRNA both targeted the same region[region 4]. It should also be noted that the references shows that siRNA was found to have low but significant correlation between the effects of siRNA and antisense. It was also found that siRNA had an IC50 value that was about 100-fold lower than that of antisense. It was also found that siRNA duplex were significantly more stable in cells than antisense or ribozymes. It was found that siRNA, like antisense compounds have different effeciencies based on the position of targeting. This was all shown in human cells before applicants invention. Applicant then discusses the examiners "attempted rebuttal" and assert that the examiner indicated that the previous declaration submitted was "not relavent". The examiner only indicated that it was not properly filed for consideration. Applicant asserts that the examiner "ignores" that Tuschl was working in Drosophila while the invention is drawn to mammals and that it is not credible to equate these two bodies of work. It has been established above that applicant is simply incorrect in this assertion.

Continuation of 13. Other: The petition filed under 37 CFR 1.48(a) has been approved. Steven Weitman will be added as an inventor. The rejection under 35USC 102(e) under Kufe et al will be withdrawn. The IDS filed 8/18/2010 has been considered.